

In the claims:

1-43. (Canceled)

44. (Currently Amended) A method of determining the existence of a pathological condition or disease predisposition in an individual or their offspring associated with a structural chromosome abnormality in a human breakpoint, comprising the steps of:

identifying a genomic nucleic acid probe sequence by ascertaining the nucleotide-by-nucleotide sequence of a target nucleic acid sequence;

comparing said ascertained sequences with the sequences of SEQ ID Nos.

1-428 and 447-479 in said target nucleic acid sequence using a computer program;

identifying a sequence that is free of SEQ ID Nos. 1-428 and 447-479 from said comparison;

developing said genomic nucleic acid probe from said identified sequence.

said identified sequence further being complementary to a non-repetitive portion of the target which hybridizes to at least a part of said identified genomic nucleic acid sequence;

providing a ~~pair of~~ separate, labeled, single copy ~~pair~~ of said genomic nucleic acid probes of ~~predetermined sequence~~ and designed to respectively hybridize on opposite sides of said breakpoint abnormality, said nucleic acid probes having at least 50 nucleotides, appearing up to three times in a haploid genome.

being free of SEQ ID NOS 1-428 and 447-479, and having a known set of sequence coordinates that define the position of said probe in reference to its location on a chromosome without a structural abnormality;

reacting said pair of probes with a chromosomal target sequence

containing said ~~breakpoint~~ abnormality, and causing the probes to hybridize to the target sequence without requiring prehybridizing or cohybridizing of said probes with unlabeled repetitive DNA sequences to provide hybridization specificity;

and

detecting said hybridized probes as a way of ascertaining the existence ~~location~~ of said ~~breakpoint~~ abnormality.

45. (Currently Amended) The method of claim 44, including a step of providing a first plurality of said separate, ~~labeled, single copy genomic~~ nucleic acid probes, each of said nucleic acid probes having at least 50 nucleotides, appearing up to three times in a haploid genome, being free of SEQ ID NOS 1-428 and 447-479, being distinct from one another and having a known set of sequence coordinates that define the position of said probe in reference to its location on a chromosome without a structural abnormality and ~~of predetermined sequence~~ designed to hybridize on one side of said ~~breakpoint~~ abnormality, and providing a second plurality of separate, ~~labeled, single copy~~ nucleic acid probes, said nucleic acid probes having at least 50 nucleotides, appearing up to three times in a haploid genome, being free of SEQ ID NOS 1-428 and 447-479, and

having a known set of sequence coordinates that define the position of said probe in reference to its location on a chromosome without a structural abnormality and of predetermined sequence designed to hybridize on the other side of said breakpoint abnormality.

46. (New) The method of claim 44, said method further including the step of localizing the genomic interval within which said abnormality exists by comparing the hybridization pattern of said first and second nucleic acid probes on a chromosome containing said abnormality with the hybridization pattern of said first and second nucleic acid probes on a chromosome without said abnormality.

47. (New) A method of detecting and localizing the interval within which a human structural chromosomal abnormality exists, said abnormality being associated with a pathological condition or disease predisposition in an individual or their offspring, said abnormality being selected from the group consisting of aneuploidy, extra or missing portions of a chromosome, and chromosomal rearrangements, said method comprising the steps of:

selecting a first and a second genomic DNA sequence by ascertaining the nucleotide-by-nucleotide sequence of a target nucleic acid sequence suspected to contain said abnormality, comparing said ascertained sequences with the sequences of SEQ ID Nos. 1-428 and 447-479 in said target nucleic acid sequence using a computer program, and identifying said first and second genomic DNA sequences from said comparison,

each said genomic DNA sequence having at least 50 nucleotides, appearing up to three times in the haploid genome, being free of SEQ ID Nos. 1-428 and 447-479, having a known set of sequence coordinates that define the position of said sequence in reference to its location on a chromosome without a structural abnormality, and being derived from the same chromosome;

hybridizing said genomic DNA sequences with a target region of human DNA having a suspected structural chromosomal abnormality without requiring prehybridizing or cohybridizing of said probes with unlabeled repetitive DNA sequences to provide hybridization specificity, said target region of DNA being from the same chromosome as said first and second genomic DNA sequences;

detecting the location of the hybridization of each of said first and second genomic DNA sequences within said target region; and

comparing said detected hybridization locations with the sequence coordinates that define the position of said sequences in reference to their location on a chromosome without a structural abnormality, and thereby determining the interval within which the abnormality occurs.

48. (New) The method of claim 47, said hybridization step using a method selected from the group consisting of Southern Blot, fluorescence *in-situ* hybridization, array comparative genomic hybridization, chromatin hybridization and bead-array genomic hybridization.

49. (New) The method of claim 47, each of said genomic DNA sequences having at least about 500 nucleotides.

50. (New) The method of claim 47, further including the step of selecting additional genomic DNA sequences, each said genomic DNA sequence having at least 50 nucleotides, appearing up to three times in the haploid genome, being free of SEQ ID Nos. 1-428 and 447-479, having a known set of sequence coordinates that define the position of said sequence in reference to its location on a chromosome without a structural abnormality, and being derived from the same chromosome.

51. (New) The method of claim 50, further including the steps of:
hybridizing said additional genomic DNA sequences with said target region of
DNA;
detecting the location of the hybridization of each of said additional genomic
DNA sequences within said target region; and
comparing said detected hybridization locations with the hybridization location of
DNA without a structural abnormality.

52. (New) A method of selecting a probe for determining the existence and or interval of a human structural chromosomal abnormality within a target region of DNA, said abnormality being associated with a pathological condition or disease predisposition in an individual or their offspring and being selected from the group consisting of

aneuploidy, extra or missing portions of a chromosome, and chromosomal rearrangements, said method comprising the steps of:

- a) relating genomic intervals in chromosomal regions to said pathological condition or disease predisposition in an individual or their offspring;
- b) selecting a first genomic DNA interval that falls within said region, said genomic interval being from DNA which does not have said abnormality and including at least one repetitive sequence having a length of at least 50 nucleotides and appearing at least 10 times in the genome of the organism;
- c) selecting a second genomic DNA interval within said first genomic interval by comparing said second genomic interval with SEQ ID Nos. 1-428 and 447-479 using a computer program, said second genomic interval having at least 50 nucleotides, appearing up to three times in the haploid genome of the organism, being free of SEQ ID NOS 1-428 and 447-479, and comprising DNA sequences from a set of known coordinates in the genome of an individual that lacks a structural chromosomal abnormality within said target region of DNA; and
- d) selecting said second genomic interval for use as said probe.

53. (New) The method of claim 52, further including the step of hybridizing said second genomic interval with said target region DNA without requiring prehybridizing or cohybridizing of said probes with unlabeled repetitive DNA sequences to provide hybridization specificity.

54. (New) The method of claim 53, said hybridization of said second genomic interval using a method selected from the group consisting of Southern Blot, fluorescence *in-situ* hybridization, array comparative genomic hybridization, chromatin hybridization, and bead-array genomic hybridization.

55. (New) The method of claim 52, said target region of DNA comprising a chromosome region of the human with the suspected chromosomal abnormality.

56. (New) The method of claim 52, each of said first and second genomic DNA intervals having at least about 500 nucleotides.

57. (New) The method of claim 52, further including the step of repeating steps a - d a second time to select a second probe.

58. (New) A method of detecting and localizing the interval within which a human structural chromosomal abnormality exists, said abnormality being associated with a pathological condition or disease predisposition in an individual or their offspring and being selected from the group consisting of aneuploidy, extra or missing portions of a chromosome, and chromosomal rearrangements, said method comprising the steps of:

selecting a plurality of genomic DNA sequences by ascertaining the nucleotide-by-nucleotide sequence of a target nucleic acid sequence suspected to contain said abnormality, comparing said ascertained sequences with the

sequences of SEQ ID Nos. 1-428 and 447-479 in said target nucleic acid sequence using a computer program, and identifying said genomic DNA sequences from said comparison, each said genomic DNA sequence having at least 50 nucleotides, appearing up to three times in the haploid genome, being free of SEQ ID NOS 1-428 and 447-479, having a known set of sequence coordinates that define the position of said genomic DNA sequence in reference to its location on a chromosome without a structural abnormality, and being derived from the same chromosome;

hybridizing said genomic DNA sequences with a target region of DNA having a suspected structural chromosomal abnormality without requiring prehybridizing or cohybridizing of said genomic DNA sequences with unlabeled repetitive DNA sequences to provide hybridization specificity, said target region of DNA being from the same chromosome as said plurality of genomic DNA sequences;

detecting the location of the hybridization of each of said genomic DNA sequences within said target region; and

comparing said detected hybridization locations with the sequence coordinates that define the position of said genomic DNA sequences in reference to its location on a chromosome without a structural abnormality, and thereby determining the interval within which the abnormality occurs.

59. (New) A method of detecting and localizing the interval within which a human nucleic acid structural abnormality exists, said abnormality being associated with

a pathological condition or disease predisposition in an individual or their offspring, said method comprising the steps of:

selecting a first and a second genomic DNA sequence by ascertaining the nucleotide-by-nucleotide sequence of a target nucleic acid sequence suspected to contain said abnormality, comparing said ascertained sequences with the sequences of SEQ ID Nos. 1-428 and 447-479 in said target nucleic acid sequence using a computer program, and identifying said first and second genomic DNA sequences from said comparison, each said genomic DNA sequence having at least 50 nucleotides, appearing up to three times in the haploid genome, being free of SEQ ID Nos. 1-428 and 447-479, having a known set of sequence coordinates that define the position of said sequence in reference to its location on a chromosome without a structural abnormality, and being derived from the same chromosome;

hybridizing said first and second genomic DNA sequences with a target region of human nucleic acid having a suspected structural abnormality without requiring prehybridizing or cohybridizing of said probes with repetitive nucleic acid sequences to provide hybridization specificity, said target region of nucleic acid being derived from the same chromosome as said first and second genomic DNA sequences;

detecting the location of the hybridization of each of said first and second genomic DNA sequences within said target region; and

comparing said detected hybridization locations with the sequence coordinates that define the position of said genomic DNA sequences in reference to their location in a nucleic acid sequence without a structural abnormality, and thereby determining the interval within which the abnormality occurs.

60. (New) A method of selecting a probe for determining the existence and or interval of a human nucleic acid abnormality within a target region of nucleic acid, said abnormality being associated with a pathological condition or disease predisposition in an individual or their offspring, said method comprising the steps of:

- a) relating nucleic acid intervals to said pathological condition or disease predisposition in an individual or their offspring;
- b) selecting a first nucleic acid interval that falls within said target region, said nucleic acid interval being from nucleic acid which does not have said abnormality and including at least one repetitive sequence having a length of at least 50 nucleotides and appearing at least 10 times in the nucleic acid sequence of the organism;
- c) selecting a second nucleic acid interval within said first nucleic acid interval by comparing said second interval with SEQ ID Nos. 1-428 and 447-479 using a computer program, said second interval having at least 50 nucleotides, appearing up to three times in the haploid genome of the organism, being free of SEQ ID NOS 1-428 and 447-479, and comprising nucleic acid sequences from a set of known coordinates in the genome of

an individual that lacks a structural nucleic acid abnormality within said target region of nucleic acid; and

d) selecting said second interval for use as said probe.

61. (New) The method of claim 44, said probes being labeled.

62. (New) The method of claim 47, said genomic DNA sequences being labeled.

63. (New) The method of claim 52, said probe being labeled.

64. (New) The method of claim 58, said genomic DNA sequences being labeled.

65. (New) The method of claim 59, said genomic DNA sequences being labeled.

66. (New) The method of claim 60, said genomic DNA sequences being labeled.